Comparison of intravenous digital subtraction angiography with radionuclide ventilation-perfusion lung scanning in patients with suspected pulmonary embolism

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ABSTRACT Fifty one patients with suspected pulmonary embolus were studied by radionuclide ventilation-perfusion scanning and intravenous digital subtraction pulmonary angiography. In 31 patients the results of both investigations were reported as negative and in a further 11 both results were reported as positive, giving a concordance rate of 82.3%. In nine patients there was disagreement between the two investigations and an attempt to resolve this difference on the basis of clinical data was made. On this basis digital subtraction angiography would have falsely classified three patients as not having an embolus who were correctly identified by radioisotope scanning. Angiography would, however, have correctly classified four patients misclassified by ventilation-perfusion scanning. The relative merits of digital subtraction angiography and radionuclide lung scanning are discussed.

Confirmation of the diagnosis of pulmonary embolism remains a common but difficult clinical problem.^{1,2} Accurate and early diagnosis is important because of the considerable morbidity and mortality associated with both untreated embolisation^{3,4} and inappropriate anticoagulant treatment.^{5,6}

Radionuclide pulmonary perfusion scans are sensitive but lack specificity. Many chronic cardiac and pulmonary disorders result in perfusion abnormalities indistinguishable from pulmonary embolism.^{7,8} With the addition of ventilation studies specificity can be improved, but in the absence of a characteristic pattern of mismatched defects diagnostic accuracy may be low.^{9,10} Pulmonary angiography therefore continues to be the most specific test for the detection of pulmonary emboli. The associated morbidity (1%) and mortality (0.5%) have, however, precluded its use in most patients and it is usually reserved for those with life threatening complications in whom aggressive treatment is being considered.^{11,12}

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Digital subtraction angiography combines digital imaging with computer subtraction techniques to provide arterial images after intravenous injection of contrast medium.¹³ This technique will provide images of the pulmonary circulation after injection of contrast medium via a central venous catheter.¹⁴ It therefore avoids the additional risk of cardiac catheterisation, which is responsible for most of the complications and the deaths that follow conventional pulmonary angiography. In 31 patients who were subsequently investigated by pulmonary angiography¹⁵ digital subtraction angiography correctly identified 12 as having suffered pulmonary embolism and excluded embolic disease in a further 18. The result was falsely positive on only one occasion. In another study¹⁶ the sensitivity of digital subtraction angiography after experimentally induced gelfoam embolisation in dogs was found to be 100% if defects in parenchymal staining during the capillary phase were taken into account. Even if the more specific criteria of demonstrating vessel cut off and intravascular filling defects are used, the method compares favourably in sensitivity (75%) with radionuclide lung scanning.

We have compared intravenous digital subtrac-

tion angiography with radionuclide ventilation-perfusion lung scanning, which is the most frequently used investigative technique in patients with suspected pulmonary embolism.

Methods

Fifty one consecutive patients were studied. All were referred to the Institute of Nuclear Medicine at the Middlesex Hospital with the suspected diagnosis of pulmonary embolism and gave informed consent to additional investigation. Sixteen were hospital inpatients, 14 were outpatients and 21 were referred from outlying hospitals. The mean age of this population was 52 years, 26 were female, 21 were smokers and eight had spirometric evidence of airflow obstruction (FEV_1/FVC ratio $< 70\%$).

In all cases ventilation-perfusion lung scans and digital subtraction angiograms were performed within 24 hours of each other. Each was reported independently in the presence of a current chest radiograph but without knowledge of specific clinical details or the result of the alternative investigation. Digital subtraction angiograms were reported in groups of 15–20 by two radiologists (AM and PD) in combination and ventilation-perfusion lung scans were reported in similar groups by two nuclear medicine physicians (SG and PE). All patients were interviewed by an independent clinician (KF) and clinical features recorded.

VENTILATION-PERFUSION LUNG SCANS

Ventilation study

A Nuclear Associates xenon lung function unit was used. Each patient inhaled 222 MBq (6 mCi) xenon 133 and images were obtained of the wash in, equilibrium, and wash out phases. Three wash out images were obtained: 0–1 min, 1–3 min, 3–6 min.

Increasing image acquisition time during wash out increases the sensitivity for gas trapping. All images were obtained in a posteroanterior projection.

Perfusion study

We gave albumin macroaggregates labelled with technetium 99m (140 MBq (4 mCi)) intravenously to each patient. Six planar projections were acquired—posteroanterior, anteroposterior, right and left laterals, and right and left posterior obliques. All images were obtained with a gamma camera having a large field of view—either a General Electric Maxicamera 400 AT or a Nuclear Enterprises Mk V LF.

Ventilation-perfusion lung scans were reported according to conventional criteria. They were regarded as positive where there was one or more segmental or two or more subsegmental perfusion

defects accompanied by a normal chest radiograph and normal ventilation, and where perfusion defects were substantially larger than any corresponding radiographic abnormality with normal ventilation.

DIGITAL SUBTRACTION ANGIOGRAPHY

Digital subtraction angiography was performed with a Technicare DR960 apparatus, which has a maximum field size of 22.5 cm. The framing rate used was 1.25 per second with a matrix of 512×512 pixels.

An arm vein was selected in the antecubital fossa and a 5 Fr catheter with side and end holes was introduced by the Seldinger technique after local anaesthesia. The catheter was advanced centrally until the tip was situated in the superior vena cava. On one occasion no suitable arm vein was available and the femoral vein was punctured and the catheter tip placed in the inferior vena cava. Forty millilitres of iohexol (Omnipaque 300) 300 mg iodine/ml were injected at 25 ml per second. The patient was instructed to hold his breath in inspiration and frames of the arterial, capillary, and venous phases were recorded for later examination.

A posteroanterior view of the right lung was obtained followed by a 25° left anterior oblique view of the left lung, a 22.5 cm field being used. Further oblique views of suspicious areas were obtained after a further injection of contrast material with a 15 cm field for elucidating specific problems.

Our preliminary studies showed three characteristic abnormalities in digital subtraction angiograms: (1) Defects in the perfusion image during the capillary filling phase. During this phase of the digital subtraction angiogram, parenchymal staining is pronounced and areas of oligoemia are easily seen. Such defects may correspond to areas of radiographic abnormality (I) or they may not (II)—see figure 1. (2) Abrupt termination of pulmonary arteries with diminished peripheral perfusion (III). (3) Filling defects visible within the pulmonary arteries (IV)—figure 2.

The last two abnormalities (III and IV), which are commonly seen in experimental embolisation of the pulmonary arteries,¹⁵ were taken to be specific for pulmonary embolism. The first type of abnormality (perfusion defects) may or may not represent pulmonary emboli. To improve the specificity of such defects they were interpreted in conjunction with a chest radiograph. Multiple perfusion defects not corresponding to areas of radiological abnormality (IIb) were reported as positive for pulmonary embolism. Defects corresponding to areas of radiographic abnormality (I) and single defects which did not correspond to such areas were reported as negative (IIa).

Fig 1 Digital subtraction angiogram, posteroanterior view, showing defect in parenchymal staining at right base.

Fig 2 Digital subtraction angiogram, right anterior oblique view, with 15 cm field showing filling defect in right basal branch of pulmonary artery (same patient as fig 1).

Results

The results of the 51 digital subtraction angiograms and ventilation-perfusion lung scans are compared in table 1. In 31 patients the results of both investigations were reported negative and in 11 patients both results were reported as positive, giving a concordance rate of 82.3%. In nine patients there was disagreement between the two results. The clinical features, digital subtraction angiographic findings, and results of radionuclide ventilation-perfusion lung scans of these patients are set out in table 2. In two patients the final clinical diagnosis remained uncertain. If the final clinical diagnosis were to be accepted in those patients with strong clinical features, digital subtraction angiography would have falsely classified three patients as not having an embolism who were correctly identified as having one by ventilation-perfusion lung scanning. Angiography would, however, have correctly classified four patients misclassified by ventilation-perfusion lung scanning. In one patient with restrictive lung disease and abnormal ventilation and perfusion the angiogram was normal. Three patients were identified as having an embolism by digital subtraction angiography because of the specific finding of occlusion of a lower lobe artery. Two of these showed matched ventilation-perfusion abnormalities on radionuclide scans, presumably as the result of established pulmonary infarcts. In the third the clinical features suggested pulmonary embolism but the radionuclide perfusion scan was normal.

Of the 11 patients where both the angiograms and the ventilation-perfusion scans were positive, nine had a final clinical diagnosis that was in agreement. Where the results of both investigations were negative ($n = 31$), six had a final clinical diagnosis suggesting pulmonary embolism. All six were investigated 48 hours after the start of anticoagulant treatment.

Over the last year we have performed digital sub-

Table 1 Comparison of digital subtraction angiography (DSA) and radionuclide ventilation-perfusion (V-Q) lung scanning in 51 patients with suspected pulmonary embolism

Digital subtraction angiography		V-Q scan	
		Negative	Positive
Negative	Normal	18	2
	I*	9	3
	IIa	4	0
	Total	31	5
Positive	IIb	0	4
	III	4	5
	IV	0	2
	Total	4	11

*See under "Methods."

Table 2 Clinical and radiographic features and findings of digital subtraction angiography (DSA) and of ventilation-perfusion lung scanning (V-Q) in the nine patients in whom the two results disagreed

Age (y) and sex	Clinical features	Radiography	DSA	V-Q	Final diagnosis
79 F	1 y cough, dyspnoea	Kyphoscoliosis	NEGATIVE Normal	POSITIVE Numerous matched defects, single unmatched defect	Restrictive lung disease
50 F	48 h pleuritic pain and haemoptysis	Normal	NEGATIVE Normal	POSITIVE Single left lower zone segmental perfusion defect	Pulmonary embolism
76 F	Non-pleuritic chest pain, dyspnoea	Normal	NEGATIVE Normal	POSITIVE Single left apical perfusion defect	Equivocal
21 F	Pleuritic chest pain and haemoptysis 1 w after transatlantic flight	Left lower zone consolidation	NEGATIVE Diminished perfusion left lower zone	POSITIVE Multiple small unmatched perfusion defects	Pulmonary embolism
61 M	Pleuritic chest pain and dyspnoea 1 w after right hip replacement	Normal	NEGATIVE Normal	POSITIVE Multiple small unmatched defects of perfusion	Pulmonary embolism
69 M	Pleuritic chest pain, dyspnoea, cough, haemoptysis after myocardial ischaemic episode	Right lower zone consolidation	POSITIVE Arterial cut off and diminished perfusion right lower lobe	NEGATIVE Matched right lower zone defect	Pulmonary embolism
69 M	Left deep venous thrombosis, dyspnoea, pleuritic chest pain	Right lower zone consolidation	POSITIVE Arterial cut off and diminished perfusion right lower lobe	NEGATIVE Matched right lower zone defect	Pulmonary embolism
80 F	4 m dyspnoea, cough	Raised right hemidiaphragm	POSITIVE Arterial cut off and diminished perfusion right lower zone	NEGATIVE Right basal perfusion defect with gas trapping	Equivocal
30 F	Iliac vein thrombosis, sudden onset of dyspnoea	Normal	POSITIVE Arterial cut off and diminished perfusion left lower zone	NEGATIVE Normal	Pulmonary embolism

traction pulmonary angiography in three seriously ill patients from the intensive therapy unit. All were too ill for ventilation-perfusion scans or any attempt at a breath holding manoeuvre: nevertheless images of diagnostic quality were obtained. In two of these the presence and distribution of emboli was subsequently confirmed at postmortem examination.

Discussion

In our 51 subjects digital subtraction angiography proved a satisfactory method of imaging the pulmonary vasculature. The diagnostic information provided was in close agreement with that provided by the conventional diagnostic technique of ventilation-perfusion lung scanning (concordance 82.3%)

Our study was performed in an unselected group of patients in whom the physicians concerned with their care suspected pulmonary embolism. Many were outpatients and others had been referred from outlying hospitals, to return the same day. In view of the significant morbidity (1.0%) and mortality (0.5%) rates associated with pulmonary angiography,¹² we did not think it ethically justifiable to proceed with this investigation in these patients. In the absence of the absolute standard of pulmonary angiography, we cannot be certain which of those

patients in whom the results of the two investigations disagreed had suffered pulmonary embolism. In the absence of such an absolute standard an attempt was made to look at the two results in the light of the final clinical diagnosis. If this clinical diagnosis is accepted digital subtraction angiography would have falsely classified as not having embolism three patients identified as having it by ventilation-perfusion scanning. All three of these patients had small peripheral perfusion defects on the radionuclide scan that were not seen on the angiogram. Digital subtraction angiography would, however, have correctly classified four patients misclassified by radionuclide lung scanning. One of these patients had pre-existing lung disease, in which the specificity of ventilation-perfusion lung scans is often low.⁹ In another two patients with the firm clinical diagnosis of pulmonary embolism digital subtraction angiography showed occlusion of the right lower lobe artery. The ventilation-perfusion scan demonstrated a matched right lower lobe defect, presumably the result of an established pulmonary infarct. Digital subtraction angiography will therefore identify those patients with established pulmonary infarcts and matched ventilation-perfusion abnormalities on radionuclide lung scans and there may be specific features on the angiogram confirming pulmonary embolism in those patients with pre-existing lung

disease in whom ventilation-perfusion lung scans may not be diagnostic. The sensitivity of digital subtraction angiography at the present time, however, is such that it may miss very small peripheral perfusion defects that are visible on radionuclide perfusion scans.

Digital subtraction angiography with its requirement for central placement of the venous catheter is more invasive than radionuclide lung scanning. In our hands it has, however, proved an acceptable and well tolerated procedure. There were no complications in these patients, nor have there been any in nearly 700 patients having digital subtraction angiography for other reasons. The requirement for a 10 second breath holding period is the major limiting factor but with adequate explanation this can be achieved by all except those with the most severe cardiorespiratory disorders. Even without a breath holding manoeuvre adequate images may often be obtained in circumstances where ventilation-perfusion scans would not be possible, such as in severely ill patients.

We have found it easier to arrange digital subtraction pulmonary angiograms at short notice, particularly overnight and at weekends. Radiology departments are normally well integrated with hospital facilities and radiologists are normally on call at all times. Nuclear medicine departments tend to be more remote and may be staffed only during office hours. The provision of radionuclide scans is often further limited by the availability of radioisotopes. The costs of the two techniques are difficult to compare directly as they will depend on the exact specifications of the equipment. The initial cost of the equipment for digital subtraction angiography in our hospital was about £300 000, compared with about £200 000 for ventilation-perfusion lung scanning. Consumables for a digital subtraction angiogram are slightly more expensive than for a radionuclide scan (about £25 versus £8) but the requirement in terms of staff time is thought to be roughly equivalent. Both digital subtraction angiography and radionuclide lung scanning equipment is used for a wide variety of other diagnostic investigations and the availability of one or other technique in any particular centre is likely to depend on the wider use of the equipment. In centres where both digital subtraction angiography and radionuclide scanning are available ventilation-perfusion lung

scanning is likely to remain the investigation of first choice. In cases where radionuclide lung scans are not diagnostic digital subtraction angiography may sometimes provide a definitive diagnosis.

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